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(54) WOUND COVERING MATERIAL

(57) A wound covering material is provided which can smoothly accelerate the reproduction of a defect skin and which can be removed readily without causing the reproduced skin to be deleted together therewith.

There is provided a wound covering material comprising a non-crystalline fibroin film.

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Description

TECHNICAL FIELD

The present invention relates to a wound covering material.

BACKGROUND ART

A covering material to be applied to a skin defect section as an artificial skin is called a wound covering material and a pig skin, chitin and so on have already been developed. These materials, however, have the drawbacks that a new skin developing under an artificial skin may also be deleted together as the artificial skin is being removed upon treatment. Further, there has recently been developed a wound covering material referred to as "Dioactive CGF" and there is the less occasion that this wound covering material may delete a new skin developing under an artificial skin together when it is being removed. This wound covering material, however, is said to be slower in the speed of forming a new skin below it than a pig skin.

DISCLOSURE OF INVENTION

It is an object of the present invention to provide a wound covering material that can smoothly accelerate the reproduction of a defect skin and that can be removed without causing a new skin developing under it to be deleted together therewith.

As a result of extensive studies and research to achieve the object as described hereinabove, the present invention have been completed on the basis of this finding.

More specifically, the present invention provides a wound covering material comprising a non-crystalline fibroin film.

The wound covering material (hereinafter referred to sometimes as a "covering material", too) according to the present invention can be prepared by using an aqueous fibroin solution as a raw material and processing it into a film.

For the preparation of an aqueous fibroin solution, a silky substance is purified by removing sericin. The silky substance may include, for example, cocoons, cocoon thread, silk yarn, silk cloth and waste thereof. The purification of the silky substance may be carried out, for example, by boiling the silky substance in an enzyme or in an aqueous solution of an alkali such as sodium carbonate, sodium hydrogen carbonate or the like, washing the resulting silky substance with water, and immersing it in warm water, thereby causing chemical substances such as sericin, sodium carbonate and so on to be eluted and removing them. It is preferred that the purified silky substance is then sterilized with ethylene oxide gas or in autoclave or by any other means.

The silky substance purified in the way as described hereinabove is then dissolved in pure water containing a dissolution aid. The dissolution aid to be employed in this case may include, for example, an acid, a neutral salt such as calcium chloride, lithium bromide or the like or ethanol.

The aqueous solution in which the silky substance is dissolved is subjected to dialysis by means of a semipermeable membrane tube or the like, thereby yielding an aqueous fibroin solution from which the dissolution aid has been removed.

The concentration of fibroin in the aqueous fibroin solution may be 2 % by weight or higher, preferably 5 % by weight or higher, although it is usually in the range of from 5 % to 20 % by weight. The rate of impurities other than fibroin in the aqueous fibroin solution may be 0.001 % by weight or lower, preferably 0.0001% by weight or lower. In this case, there is the possibility that sericin, chlorine or the like may be contained as impurities.

The process of forming the aqueous fibroin solution into a film may comprise casting the aqueous fibroin solution on a flat and smooth surface of a solid member and removing the water contained therein by evaporating it. It is of great importance in this case that a resulting fibroin film is not made crystalline and that it becomes a substantially non-crystalline film. In order to achieve this, it is preferred to adjust a speed of removing the water by evaporation from the aqueous fibroin solution in the process of filming it and it is possible to prevent a crystallization of the resulting film by making the speed of evaporating the water faster.

The crystallization of the fibroin film is caused to occur in the process of drying the aqueous fibroin solution when it takes a longer time to dry it in such a state that the concentration of the aqueous fibroin solution becomes 30 % or higher. In order to prevent the crystallization of the fibroin film, the aqueous fibroin solution may be dried at 0.5 atmospheric pressure or lower, preferably 0.1 atmospheric pressure or lower, when the drying is carried out at reduced pressure. When the drying is carried out at ambient pressure, it is necessary to alter the temperature, humidity and wind velocity of gaseous fluid such as air or inert gas (nitrogen gas or the like) in a drying chamber. The temperature at which the aqueous fibroin solution is formed into a film may range from 0°C to 50°C, preferably from 10°C to 30°C. The relative humidity RH of air or such inert gas may range from 40 % to 90%, preferably from 50 % to 80 %. It is preferred that the aqueous fibroin solution is formed into a film by bringing a film of the fibroin solution cast on the solid surface into contact with air or the inert gas (nitrogen gas or the like) having a temperature in the range of from 0°C to 50°C, preferably from 10°C to 30°C at the wind velocity of 5 cm per second or higher, preferably from 10 cm per second to 30 cm per second. When it is intended to prepare a fibroin film having the film thickness of 30 μm or thicker, particularly in the range of from 40 to 60 μm, it is preferred that the wind velocity of the air or inert gas is defined at 10 cm per second or higher

or the relative humidity is set to be approximately 30 RH at the wind velocity of about 10 cm per second or lower, thereby preventing the crystallization of the resulting fibroin film.

For the fibroin film to be employed as a covering material in accordance with the present invention, the film thickness may be set to be in the range of from 20 μm to 80 μm. The water contents of the resultant film may be in the range of from 1 % to 16% by weight, preferably from 5% to 13% by weight. The resulting fibroin film may be laminated on another film as needed.

When the covering material is actually employed, it is preferred to sterilize it with ethylene oxide gas prior to use.

Examples

The present invention will be described in more detail by way of example.

Example

(1) Preparation of a raw material

Raw silk yarn was boiled in a 0.5 % (by weight) sodium carbonate aqueous solution for 1 hour, washed with water and immersed in a warm water at 60°C for 30 minutes to thereby remove sericin and sodium carbonate. The resulting silk yarn was sterilized in autoclave and it is employed as a raw material for preparing a fibroin film.

(2) Dissolution of silk yarn

The purified silk yarn prepared in the step (1) above was dissolved in an aqueous solution consisting of water, calcium chloride and ethanol (mixed molar ratio = 1 : 2 : 8). The weight rate of the silk yarn with respect to the aqueous solution was adjusted to be 1 : 7. The resultant aqueous solution was filled in a cellulose tube (a semipermeable membrane) and subjected to dialysis with pure water, thereby yielding an aqueous fibroin solution. The concentration of fibroin in the resultant aqueous fibroin solution was found to be approximately 7 % by weight.

(3) Preparation of a fibroin film

The resulting aqueous fibroin solution was cast in a given area on a flat plastic plate and dried while feeding air at the wind velocity of from 20 to 40 cm per second in a chamber having the temperature of 20°C and the relative humidity of 65 % RH. Although the film thickness of the fibroin film may vary with the concentration and the amount of the aqueous fibroin solution and the area of a film surface to be dried, it is set to become 20 μm or thicker in this case. Further, the wind velocity is set to be faster as the resulting film becomes thicker because the film becomes more crystalline as it is thicker.

(4) Properties of the fibroin film

From the fact that an X-ray diffraction photograph of the resultant fibroin film shows an amorphous halo, it is confirmed that fibroin is non-crystalline. In order to determine a solubility of the resulting fibroin film in water (at room temperature), the fibroin film was dissolved in water at room temperature and, as a result, it is found that the resultant fibroin film has been dissolved almost fully in water in several minutes. From this result, it is further confirmed that the resulting fibroin film is substantially non-crystalline.

Furthermore, in order to determine an interaction of the fibroin film with blood, one droplet of blood was dropped onto the film. As a result, the blood was absorbed within one minute and the film became swollen. This indicates that the resulting non-crystalline fibroin film has a good interaction with a body liquid and the body liquid is adsorbed thereon very well while water is likely to be evaporated therethrough.

(5) Functions as a wound covering material

In order to determine the functions of the non-crystalline fibroin film as a wound covering material, the film was applied to a fire-burnt site after it has been sterilized with ethylene oxide gas. As a result, it is found that the film absorbed the body liquid excreted from the body and the water was allowed to be evaporated from its surface, thereby keeping the wound site in a dry state. It is further found that the resulting film allowed a new skin to be created at the wound site even when it has been applied to the site without exchanges for a week. From this result, it is confirmed that the fibroin film has demonstrated the sufficient functions as an artificial skin.

The wound covering material according to the present invention presents the advantages that the reproduction of a defect skin and the creation of a new skin can be accelerated by covering the surface of a defect (wound) skin with this wound covering material as an artificial skin and that the film can be removed without causing the reproducing defect skin and the developing new skin to be deleted together therewith. Further, when the wound covering material according to the present invention is applied to the defect skin, it further has the merits that it does not require exchanges over a long period of time.

Claims

1. A wound covering material comprising a non-crystalline fibroin film.

2. A wound covering material as claimed in claim 1, wherein a water content of said non-crystalline

fibroin film ranges from 1% to 16% by weight.

3. A wound covering material as claimed in claim 1 or 2, wherein a film thickness of said non-crystalline fibroin film ranges from 20 μm to 80 μm.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP97/00144

A. CLASSIFICATION OF SUBJECT MATTER
Int. Cl^6 A61L15/01, 27/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int. Cl^6 A61L15/01, 27/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP, 56-40156, A (Kanebo, Ltd.), April 16, 1981 (16. 04. 81)(Family: none)	1 - 3
Y	JP, 56-34349, A (Kanebo, Ltd.), April 6, 1981 (06. 04. 81)(Family: none)	1 - 3
Y	JP, 2-109570, A (Sumie Orimono K.K.), April 23, 1990 (23. 04. 90)(Family: none)	1 - 3
Y	JP, 2-233128, A (Director General of National Institute of Sericultural and Entomological Science, Ministry of Agriculture, Forestry and Fisheries), September 14, 1990 (14. 09. 90)(Family: none)	1 - 3

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
March 19, 1997 (19. 03. 97)	April 1, 1997 (01. 04. 97)
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